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INTRODUCTION

A well-organized network of laboratories, capable of rapidly and correctly identifying and subtyping influenza viruses is critical to recognizing and managing an influenza pandemic. Recognition of novel strains of influenza virus will be dependent upon early detection and sampling of initial clinical cases associated with the pandemic. Since the symptoms of influenza are nonspecific and are similar to those caused by a number of respiratory pathogens, laboratory testing must be performed to identify the causative agent as a form of the influenza virus.

Routine testing of human specimens for the presence of microbial agents is an activity that places all clinical laboratories in a position to serve in a "sentinel" capacity. By default, these laboratories will be at the front line for detecting the first clinical cases of novel influenza strains, such as H5N1 avian influenza.

It is essential that the Missouri State Public Health Laboratory (MSPHL) be prepared to deal with novel influenza strains. The MSPHL will work with the Centers for Disease Control (CDC) to monitor year-round influenza subtypes and to detect new subtypes through laboratory-based surveillance. MSPHL will also provide advanced testing, unavailable at the sentinel level, including viral culture, molecular detection and subtyping of viral isolates. In the event of an influenza pandemic, the MSPHL will work with CDC to provide guidelines for specimen management and diagnostic testing as the pandemic evolves.

Trainings and exercises are part of the preparedness activities that MSPHL participates in throughout the year. Every month MSPHL exercises the laboratory influenza-testing plan by testing scientist's competencies in polymerase chain reaction (PCR) testing. The Missouri Department of Health and Senior Services' (DHSS) MSPHL, Bureau of Communicable Disease Control and Prevention and Bureau of Immunization Assessment and Assurance in cooperation with local public health agencies (LPHAs) perform year round, outbreak and seasonal influenza surveillance. In support of this influenza surveillance, MSPHL and program staff conduct training sessions each year at DHSS area or district health offices. Such training provides hands on opportunities for health care professionals to ask questions and gain knowledge on issues related to seasonal , avian and pandemic influenza; data collection and interpretation; laboratory testing issues; and vaccinations. These trainings serve as an opportunity to review packaging and shipping protocols, reporting mechanisms, and responsibilities.

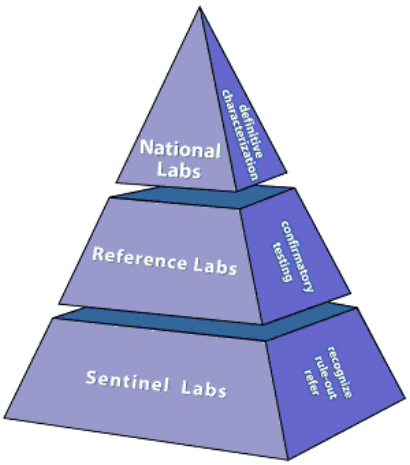
MSPHL in cooperation with the Council of State and Territorial Epidemiologists (CSTE) and other DHSS staff conducted six training exercises throughout the state of Missouri. Specialists in epidemiology, emerging diseases, laboratory, and veterinary public health attended these training exercises. Participants learned: to recognize and manage a human case of Highly Pathogenic Avian Influenza (HPAI); comprehend laboratory diagnosis and specimen collection; and review the investigation process of a possible human-to-human HPAI transmission. Finally, those attending the trainings participated in an exercise and case study to allow participants to walk through an investigation and response to HPAI detection among poultry.

Other aspects of the Laboratory Pandemic Plan are exercised while participating in the DHSS' Disaster Situation Room drills that are held annually.

PLANNING ASSUMPTIONS

- As part of the National Laboratory Response Network (LRN), the MSPHL will utilize approved LRN testing methods for influenza specimens during all Phases of a pandemic, or as instructed by CDC.
- MSPHL will follow all testing algorithms as disseminated by CDC (i.e., once pandemic strain is identified in a region, testing efforts may be focused to other regions as the pandemic evolves).
- MSPHL will continue to conduct year-round testing for influenza viruses in order to characterize circulating influenza strains and to monitor for novel influenza subtypes.
- MSPHL maintains testing supplies and has the capacity to meet the public health surveillance needs of the state. MSPHL is not a diagnostic influenza testing site and does not accept specimens that are not of public health significance.
- MSPHL scientists are cross-trained in an effort to assist with testing of greatest need. There is an acknowledgement that certain testing may be delayed or redistributed to other laboratories in order to meet more pressing or other critical testing demands.
- MSPHL will utilize the Missouri LRN (MOLRN) to contact member laboratories throughout the state with up-to-date testing recommendations and information.
- The Mid-America Alliance will be a resource for laboratory surge capacity.

BACKGROUND



LRN became operational in August 1999 with the objective to ensure an effective laboratory response to bioterrorism. The LRN is an integrated network of local clinical laboratories (sentinel labs), state and local public health laboratories (reference labs) and federal laboratories (CDC, The United States Army Medical Research Institute for Infectious Diseases, Food and Drug Administration). MOLRN is a network of Missouri laboratories that are fully equipped and trained to respond quickly to acts of chemical or biological terrorism, emerging infectious diseases, and other public health threats and emergencies. MOLRN includes MSPHL, which serves as Missouri's LRN reference laboratory, plus sentinel laboratories within the state. See http://www.bt.cdc.gov/lrn/biological.asp.

SENTINEL LABORATORIES

According to the 2008 MOLRN survey of sentinel laboratories within Missouri, 81% perform rapid diagnostic testing for influenza viruses on respiratory specimens. Of these, 9% have the capability to perform high-complexity viral testing, including the use of viral isolation techniques. In addition, 6% of Missouri's sentinel laboratories are capable of performing PCR or immuno-fluorescence (IF) testing for rapid detection and sub-typing. These laboratories could be utilized for surge capacity should the situation warrant the need. *Hospital laboratories should not attempt to isolate influenza viruses from patients with suspected novel influenza virus infections.* Fifty-two percent (52%) of Missouri's sentinel laboratories have participated in some sort of pandemic influenza planning, but 75% of those who participated in pandemic influenza planning had not exercised the plan. Twelve percent (12%) of responding laboratories indicated they had participated in internal exercises conducted by their laboratory or hospital, and 8% have participated in external exercises conducted by a state or local agency. Only 5% responded that they had participated in both internal and external exercises.

MISSOURI STATE PUBLIC HEALTH LABORATORY, TESTING CAPABILITIES

- MSPHL maintains a fully trained technical virology staff. In the summer of 2007, MSPHL moved into a new state-of-the-art facility that contains an extensive biosafety level 3 (BSL-3) laboratory. Additional scientists have been trained in PCR testing to provide back-up and support during a pandemic or public health emergency.
- MSPHL is a collaborating laboratory in the World Health Organization's Global Influenza Surveillance Network. Year-round respiratory specimens from designated sentinel laboratories are sent to the MSPHL where they are tested by viral culture. The resulting isolates are subtyped by hemagglutination/ hemagglutination inhibition (HA/HAI) testing. A representative sample of these seasonal isolates, along with isolates that cannot be typed and those from vaccine failures, are forwarded to CDC for further testing. Weekly reports of laboratory-confirmed cases of Influenza A and B viruses, by age group, are sent to CDC via the Public Health Laboratory Information System (PHLIS).
- MSPHL participates in year-round laboratory-based surveillance via the National Respiratory and Enteric Virus Surveillance System (NREVSS).
- MSPHL maintains year-round capability to perform real time polymerase chain reaction (RT-PCR) testing for influenza A (subtyping: H1, H3, H5 [HP Asian lineage]) and B viruses using the protocols for state public health laboratories developed by CDC and distributed through the Association for Public Health Laboratories (APHL) MSPHL can also perform an additional, recently released RT-PCR test to detect the highly pathogenic A/H5 (Asian Lineage) virus. New assays will be added as they are validated and released by CDC through APHL for LRN laboratories.
- MSPHL continues to participate in the LRN proficiency-testing program, the College of American Pathologists (CAP) proficiency-testing program and the CAP bioterrorism proficiency testing program and will maintain its status as a certified laboratory within the Select Agent Program.
- As part of the LRN, MSPHL has the capability of transferring samples to the nearest appropriate partner laboratory if the laboratory cannot perform the required tests or becomes overwhelmed.

- MSPHL is also a collaborating laboratory in the Mid-America Alliance whose mission is to provide mutual assistance among states during a situation that stresses individual states resources. Should testing needs overwhelm current capacity, MSPHL will utilize the Mid-America Alliance.

PANDEMIC INFLUENZA: LABORATORY ROLES AND RESPONSIBILITES

Sentinel and Other Private Laboratories:

Pandemic Alert Period: Phases 4 and 5

- Inventory current levels of diagnostic supplies, including personal protective equipment; assess anticipated needs for equipment and supplies, and determine trigger point for ordering additional resources. Consider a back-up source for supplies.
- Identify key laboratory personnel whose roles are critical to maintaining laboratory operations.
- Train employees in management of respiratory specimens.
- Institute surveillance for flu-like illnesses among laboratory personnel.
- Cross-train employees to perform rapid diagnostic tests and report results.
- Qualified personnel should be identified to staff laboratory for 24/7 capabilities.
- Ensure employees are trained in the proper packaging and shipping of suspected novel influenza strains to MSPHL.
- Follow current DHSS guidelines for testing and reporting of persons with suspected infection with a novel strain of influenza virus. See http://www.dhss.mo.gov/BT_Response/HUDUpdatedH5N1TestingGuidance06-19-06.pdf and companion document http://www.dhss.mo.gov/Lab/Virology/RespiratoryVirusTesting.html.

Pandemic Alert Period: Phase 6

- Follow updated DHSS guidelines for testing and reporting of persons with suspected infection with a novel strain of influenza virus, as pandemic evolves. See http://www.dhss.mo.gov/BT_Response/HUDUpdatedH5N1TestingGuidance06-19-06.pdf and companion document. http://www.dhss.mo.gov/Lab/Virology/RespiratoryVirusTesting.html.
- Scale up to manage increased requests for influenza testing.
- Continue to expedite specimens from possible pandemic influenza patients to MSPHL
- Maintain surveillance for flu-like illnesses among laboratory personnel.

Missouri State Public Health Laboratory

Pandemic Alert Period: Phases 4 and 5

- Maintain frequent contact with CDC for guidance related to the novel virus, including institution of new testing algorithms, changes in procedures, availability of testing reagents, etc. as pandemic evolves. Testing protocols will be dictated by CDC algorithms and may be modified with each stage of the pandemic**.** Testing protocols are restricted to

state and local public health laboratories in the LRN and are distributed through APHL. CDC provides testing reagents solely to LRN laboratories.

- Inventory current levels of supplies, assess anticipated needs for equipment and supplies and determine trigger point for ordering additional resources. Include specimen mailing kits in assessment. Arrange for back-up manufacturer source for supplies and equipment.
- Enhance lab-based influenza surveillance by increasing designated sentinel sites.
- Educate sentinel laboratories, LPHAs, physicians and other network partners on how to contact MSPHL if novel influenza is suspected.
- Cross-train MSPHL technicians during regular flu season to perform rapid tests, LRN-validated RT-PCR procedures and to report results. Scale up as requests for influenza testing increase.
- Employ and train temporary staff to perform rapid tests, LRN-validated RT-PCR procedures and to report results. Scale up as requests for influenza testing increase.
- Institute surveillance for flu-like illnesses among laboratory personnel.
- Educate sentinel laboratories within Missouri which have BSL 3 facilities on the highly pathogenic nature of avian influenza A (H5N1); the H5N1 virus should be manipulated only in BSL3+ (enhanced) environment. Respiratory virus cultures should not be performed in most clinical laboratories and such cultures should not be ordered for patients suspected of having H5N1 infection. See http://www.cdc.gov/flu/h2n2bsl3.htm.
- Supply updated information received from CDC on an ongoing basis to MOLRN laboratories, LPHAs and other associated partners using Health Alerts, MOLRN broadcasts, updated website information and by other communication means as necessary. See http://www.dhss.mo.gov/Lab/Virology/RespiratoryVirusTesting.html.
- Continue ongoing training of sentinel laboratories and LPHAs in proper specimen collection, handling and packaging and shipping procedures. See http://www.dhss.missouri.gov/Lab/Virology/sphl_avianflu_instructions.pdf .
- Communicate expeditiously to the DHSS Division of Community Public Health (DCPH) any confirmation of the novel virus within the state.
- Continue to supply sampling kits and maintain courier service to all counties to facilitate receipt of novel influenza strain at the MSPHL.

Pandemic Alert Period: Phase 6

- Utilize technicians cross-trained during regular flu season to perform rapid tests, LRN-validated RT-PCR procedures and to report results as requests for influenza testing increases.
- Utilize temporary staff as needed to meet increased staffing needs.
- Maintain frequent contact with CDC for guidance related to the novel virus, including institution of new testing algorithms, changes in procedures, availability of testing reagents, etc. as pandemic evolves.
- Supply updated information received from CDC on an ongoing basis to MOLRN laboratories, LPHAs and other associated partners using Health Alerts, MOLRN broadcasts, updated website information and by other communication means as necessary. See http://www.dhss.mo.gov/Lab/Virology/RespiratoryVirusTesting.html.
- Communicate expeditiously to the DCPH, initial confirmation of the novel virus within the state and trends and movement of the virus throughout the state as the pandemic evolves.

- Continue to supply sampling kits and maintain courier service to all counties to facilitate receipt of novel influenza strain at the MSPHL

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- CDC Pandemic Influenza website: http://www.pandemicflu.gov/

- WHO Influenza Network website: http://www.who.int/csr/disease/influenza/influenzanetwork/en/index.html

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